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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,111	05/14/2001	Louis Schofield	18861	1473

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/787,111	SCHOFIELD, LOUIS	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 54-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 54-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendments filed January 9, 2006 and May 20, 2005 are acknowledged and have been entered. Claims 1-37 and 39-53 have been canceled. Claims 59-61 have been amended. Claims 38 and 54-61 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 54-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite in the recitation of "insufficient"; what are the metes and bounds of insufficient? How much of the lipidic domain can still remain yet an immune response be achieved?

The rejection is maintained for the reasons of record. Applicant's arguments filed May 20, 2005 have been fully considered but they are not persuasive.

"Applicant respectfully submits that the claims clearly delineate that the extent of the lipidic domain that remains in the modified GPI molecule is such that the residual lipidic domain, if any, is insufficient to induce or elicit an immune response to a GPI lipid domain. Applicant respectfully submits that in light of the teaching in the specification, the meaning of the recitation "insufficient" is clear to those skilled in the art. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is therefore respectfully requested." (Remarks, p. 6) However, the requirement under 112, second paragraph is that the claim be definite, particularly pointing out and distinctly claiming the subject matter which applicant regards as the invention. The term "insufficient" is not a definite term. What are the metes and bounds of this term? The scope of the claim with regard to "insufficient lipidic domain to induce or elicit an immune response directed to a GPI lipid domain", the phrase is not defined. How much GPI lipid domain is removed from the modified GPI such that there is no immune response to the GPI lipid domain induced or elicited?

4. Claims 38 and 54-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Tachado et al 1997 (PNAS, USA, 94:4022-4027) or Schofield et al 1996 (Journal of Immunology, 156:1886-1896).

Tachado et al 1997 discloses GPI anchored surface proteins and mAb to the GPI (abstract). The prior art discloses a diluent (water). Tachado et al 1997 discloses derivatives or precursors of the GPI (materials and methods).

Schofield et al 1996 discloses a GPI of malaria parasite origin and in PBS, water or buffer of choice (abstract; p. 1887). Schofield et al 1996 discloses mAb to malarial GPI (p. 1887).

Although the prior art does not specifically disclose that the lipidic domain is incapable of inducing an immune response, it would appear that the no immune response is induce directed to the lipidic domain of said GPI.

Further, it is noted that the specification defines derivatives and equivalents "...to be understood to include fragments, parts, portions, chemical equivalents, mutants, homologs and analogs. Chemical equivalents of a GPI inositolglycan domain can act as a functional analog of the GPI inositolglycan domain. For example, a chemical equivalent of the GPI inositolglycan domain includes a GPI inositolglycan domain in which the phosphoglycerol component of the inositolglycan has been modified to increase hydrophobicity. This may be achieved by replacement with truncated, partial or modified fatty acids or other hydrophobic moieties and acts to improve the immunogenicity or stability of the molecule, without generating an undesirable antibody response. Chemical equivalents may not necessarily be derived from a GPI inositolglycan domain but may share certain conformational similarities. Alternatively, chemical equivalents may be specifically designed to mimic certain immunological and physiochemical properties of the GPI inositolglycan domain. Chemical equivalents may be chemically synthesised or may be detected following, for example, natural product screening. Chemical equivalents also include synthetic carbohydrates and peptide mimics. Homologs of GPI inositolglycan domains contemplated herein include, but are not limited to, GPI inositolglycan domains from different species including, for example, Saccharomyces. Fragments, include portions such as the glycan component of the inositolglycan domain, which portions are effective in achieving the object of the present invention." (see specification pp. 15-16).

It would appear that the prior art discloses the claimed GPI molecule. Since the Patent Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

With regard to the prior art rejection, it is noted that the reference discloses the composition and that the function (induces an immune response directed to a micro-organism GPI inositolglycan domain but is incapable of inducing an immune response directed to a lipidic domain of said GPI) or properties are inherent so long as the claimed product components are disclosed in the prior art. Further, it is noted that Applicant is not claiming a method of inducing an immune response, but rather a product, a modified GPI, which the prior art discloses. The "modified GPI molecule or derivative or equivalent thereof" is not specifically defined.

Since the Patent Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

The rejection is maintained for the reasons of record. Applicant's arguments filed May 20, 2005 have been fully considered but they are not persuasive.

Applicant has asserted that the references merely disclose intact GPI molecules or precursors thereof and that the reference does not teach or suggest, implicitly or explicitly, a modified GPI molecule that lacks the lipidic domain and that induces an immune response against the glycan domain of the molecule and does not induce an immune response to the lipid domain of the intact GPI. However, it is noted that the prior art discloses precursors of the GPI and that there was some minor batch-to-batch variability in contamination with lipids (Tachado et al, p. 4023). A precursor would appear to be a derivative or equivalent thereof. As previously stated, neither the claims nor the specification clearly define derivatives or equivalents. The specification states that they are understood to include fragments, parts, portions, chemical equivalents, mutants, homologs and analogs. Therefore, a precursor would appear to be a fragment, part or portion. The rejection is maintained.

5. Claims 38 and 54-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. At present the pending claims specifically recite a composition, however a reading of the specification appears to indicate that Applicants intend to use these compositions as vaccines. The specification contemplates that the composition can be used in treatment and/or prophylaxis of mammal disease condition (i.e. malaria) and a vaccine composition (see pp. 7-8). Claim 38 is directed to a composition comprising modified GPI molecule or derivative or equivalent thereof which induces an immune response directed to a

microorganism GPI inositolglycan domain but is incapable of inducing an immune response directed to a lipidic domain of said GPI. Other claims specifically define domain structure and specifically the 4 amino acids in claim 60 for example.

The specification teaches in Example 16, p 66, that all of the mice died (control and experimental) when immunized with free GPI upon challenge with *P. berghi*. The immunization of mice with free GPI generates IgM reacting with PI domain of GPI. The immunization appears to exacerbate the *P. berghi* cerebral malaria syndrome. Exacerbated pathogenicity by increase death rate was observed upon passive transfer of IgM mAb. And finally that mAb cross-react with host GPI by FACS analysis. Example 17 of the specification on page 67 teaches that immunization of mice with GPI-glycan-KLH and IFA protected 57% of mice upon parasite challenge. Also the specification indicated that passive immunization was successful, 95% protection when mice were immunized with anti-GPI glycan-KLH. 100% of the control mice died.

In view of the above examples, it would appear that the specification does not enable the claimed invention of a composition that only comprises a modified GPI. The claims do not define how the GPI has been modified. The specification indicates that free GPI does not protect against Plasmodium infection. It appears free GPI behaves in the same manner as the controls. The specification is not enabled for any of the specifically claimed GPIs as set forth in claims 59-61. The specification is not enabled foe the modified GPI molecule as claimed with the defined 4 amino acids or the specific GPI inositolglycan domain. The state of the art teaches that GPI anchor moieties or modification have not been successful in the treatment or protection against malaria. Gowda et al states that "[D]epsite the possibility that detailed knowledge of the parasite GPI anchor structure, function

and biosynthesis could provide attractive targets for anti-malarial drug development, such studies have not received wide attention. If GPI anchors are pathogenicity factors, the precise molecular mechanism of action of the host needs to be established, as does the GPI biosynthesis pathway. Other aspects that remain unanswered are: (1) the identity and significance of the unusual substituents on the glycan moieties of *P. falciparum* protein GPI anchors; (2) whether GPI anchors are involved in membrane modifications that occur during the parasite invasion of red blood cells and in exporting functional proteins to the erythrocyte surface; (3) whether the parasite GPI anchors released into the host bloodstream contribute to immune-mediated cell lysis, a possible cause of tissue injury; and (4) whether anti-GPI anchor moieties are involved in host anti-disease immune response." (see p. 151, col. 1).

In view of the lack of enablement in the specification and the state of the art, the claimed invention is not enabled and would require undue experimentation for a skilled artisan to practice the claimed invention.

The rejection is maintained for the reasons of record. Applicant's arguments filed May 20, 2005 have been fully considered but they are not persuasive. It is noted that the specifically claimed compositions are not enabled. It is noted that Applicant has described the function of the modified GPI, however, the structure of the modified GPI is not set forth in the claims.

6. No claims are allowed.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR

only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
December 11, 2006